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LE COVERS 1907 - 5 Mar 2003 VOL 138 ISS 10
LE LAST UPDATED: 4 Mar 2003 (20030304/ED)

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liposome same imexon
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s liposomes (p) imexon
34400 LIPOSOMES
22 IMEXON
1 LIPOSOMES (P) IMEXON

d 1 kwic

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
Drug delivery systems
(liposomes; liposomal compns. comprising imexon
derivs.)

d 1 bib ab

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

2002:408506 CAPLUS

137:10970

Liposomal compositions comprising imexon derivatives

Lopez-Berestein, Gabriel; Remers, William A.; Hersh, Evan M.

Board of Regents, the University of Texas System, USA; Arizona Board of

Regents, University of Arizona

PCT Int. Appl., 106 pp.

CODEN: PIXXD2

Patent

English

N.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002041871	A2	20020530	WO 2001-US43292	20011120
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

AU 2002016672 A5 20020603 AU 2002-16672 20011120

AI US 2000-721040 A1 20001121

WO 2001-US43292 W 20011120

Disclosed are novel compns. comprising a lipid and imexon or a deriv. thereof. Also disclosed are liposomal compns. comprising imexon or deriv. thereof. Methods for administering pharmaceutically acceptable compns. comprising a lipid and imexon or a deriv. thereof for the treatment of diseases, such as cancer, are also disclosed herein. Thus, 2-cyanoaziridine-1-(N-methyl)carboxamide (I) was prepd. by the reaction of 2-cyanoaziridine with Me isocyanate. Antitumor activity of liposomal I was tested against a panel of tumor cells in culture.

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ENTRY	SESSION

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E COVERS 1907 - 5 Mar 2003 VOL 138 ISS 10

E LAST UPDATED: 4 Mar 2003 (20030304/ED)

his file contains CAS Registry Numbers for easy and accurate ubstance identification.

s-imexon (p) lipid?
22 IMEXON
288161 LIPID?
1 IMEXON (P) LIPID?

d 1

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
2002:408506 CAPLUS
137:10970
Liposomal compositions comprising imexon derivatives
Lopez-Berestein, Gabriel; Remers, William A.; Herish, Evan M.
Board of Regents, the University of Texas System, USA; Arizona Board of
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PCT Int. Appl., 106 pp.
CODEN: PIXXD2
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AU 2002016672	A5	20020603	AU 2002-16672	20011120
AI US 2000-721040	A1	20001121		
WO 2001-US43292	W	20011120		

s imexon (p) emulsion?
22 IMEXON
210578 EMULSION?
0 IMEXON (P) EMULSION?

s imexon and phospholipid?
22 IMEXON
109542 PHOSPHOLIPID?
2 IMEXON AND PHOSPHOLIPID?

d 1-2

ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
2002:408506 CAPLUS
137:10970
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Lopez-Berestein, Gabriel; Remers, William A.; Herish, Evan M.
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AI US 2000-721040 A1 20001121
WO 2001-US43292 W 20011120

ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS

2002:95271 CAPLUS

136:395484

Molecular and cellular characterization of *imexon*-resistant

RPMI8226/I myeloma cells

Dvorakova, Katerina; Payne, Claire M.; Tome, Margaret E.; Briehl, Margaret
M.; Vasquez, Miguel A.; Waltmire, Caroline N.; Coon, Amy; Dorr, Robert T.

Arizona Cancer Center, University of Arizona, Tucson, AZ, 85724, USA

Molecular Cancer Therapeutics (2002), 1(3), 185-195

CODEN: MCTOCF; ISSN: 1535-7163

American Association for Cancer Research

Journal

English

CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

d 1-2 bib ab

ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS

2002:408506 CAPLUS

137:10970

Liposomal compositions comprising *imexon* derivatives

Lopez-Berestein, Gabriel; Remers, William A.; Hersh, Evan M.

Board of Regents, the University of Texas System, USA; Arizona Board of
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PCT Int. Appl., 106 pp.

CODEN: PIXXD2

Patent

English

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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

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Antitumor activity of liposomal I was tested against a panel of tumor
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ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS

2002:95271 CAPLUS

136:395484

Molecular and cellular characterization of *imexon*-resistant

RPMI8226/I myeloma cells

Dyprakova, Katerina; Payne, Claire M.; Tome, Margaret E.; Briehl, Margaret M.; Vasquez, Miguel A.; Waltmire, Caroline N.; Coon, Amy; Dorr, Robert T.

Arizona Cancer Center, University of Arizona, Tucson, AZ, 85724, USA

Molecular Cancer Therapeutics (2002), 1(3), 185-195

CODEN: MCTOCF; ISSN: 1535-7163

American Association for Cancer Research

Journal

English

Imexon is an aziridine-contg. iminopyrrolidone with selective growth-inhibitory potency for multiple myeloma. Our previous research indicates that **imexon** induces mitochondrial alterations, oxidative stress, and apoptosis. This drug represents an interesting model drug with a nonmyelosuppressive profile to study the basic mechanisms leading to antitumor activity and resistance. The major purpose of this study was to characterize an **imexon**-resistant RPMI8226/I cell line that was developed from RPMI8226 cells by continuous exposure to **imexon**. No significant differences were obsd. in the sensitivity to several cytotoxic drugs, including mitoxantrone, mitomycin C, melphalan, methotrexate, cytarabine, cisplatin, vincristine, and paclitaxel, in the **imexon**-resistant cells. However, RPMI8226/I cells were cross-resistant to arsenic trioxide, doxorubicin, fluorouracil, etoposide, irinotecan, and esp. IFN-.alpha.. The data from DNA microarray and Western blot analyses indicated that the levels of antiapoptotic proteins Bcl-2 and thioredoxin-2, which reside mainly in the mitochondria, are increased in RPMI8226/I cells. In addn., increased levels of lung resistance protein were detected in **imexon**-resistant cells. Expression of P-glycoprotein was not detected in RPMI8226/I cells. No loss of mitochondrial membrane potential or increase in the levels of reactive oxygen species was obsd. in RPMI8226/I cells after exposure to **imexon**; however, the levels of glutathione are increased in the RPMI8226/I cells. TEM revealed significant changes in the mitochondrial morphol. of RPMI8226/I cells, whereas no ultrastructural changes were obsd. in other cellular compartments. **Imexon**-resistant RPMI8226/I myeloma cells appear to have a unique mechanism of resistance that is assocd. with morphol. alterations of mitochondria, increased protection against oxidative stress, elevated levels of glutathione, and enhanced expression of antiapoptotic mitochondrial prot ins.

CNT 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

.mexon (p) micelle?

22 IMEXON

49009 MICELLE?

1 IMEXON (P) MICELLE?

d 1

ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

2002:408506 CAPLUS

137:10970

Liposomal compositions comprising imexon derivatives

Lopez-Berestein, Gabriel; Remers, William A.; Herish, Evan M.

Board of Regents, the University of Texas System, USA; Arizona Board of Regents, University of Arizona

PCT Int. Appl., 106 pp.

CODEN: PIXXD2

Patent

English

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
 RW: UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 AU 2002016672 A5 20020603 AU 2002-16672 20011120
 AI US 2000-721040 A1 20001121
 WO 2001-US43292 W 20011120

s imexon

22 IMEXON

d 1-22 bib ab

ANSWER 1 OF 22 CAPLUS COPYRIGHT 2003 ACS

2002:875617 CAPLUS

Imexon activates an intrinsic apoptosis pathway in RPMI8226

myeloma cells

Dvorakova, Katerina; Payne, Claire M.; Landowski, Terry H.; Tome, Margaret
 E.; Halperin, Daniel S.; Dorr, Robert T.

Dep. Microbiol. and Immunology, Univ. Arizona, Tucson, AZ, 85724, USA

Anti-Cancer Drugs (2002), 13(10), 1031-1042

CODEN: ANTDEV; ISSN: 0959-4973

Lippincott Williams & Wilkins

Journal

English

Imexon is a new antitumor agent with high activity in multiple myeloma. This drug induces apoptosis, oxidative stress and mitochondrial alterations. However, it was unknown whether **imexon** activates an intrinsic apoptotic pathway that is assocd. with activation of caspase-9 or an extrinsic pathway that is induced by receptor-mediated signals such as Fas ligand characterized by caspase-8 activation. In addn., we wanted to investigate the effect of **imexon** on Bcl-2 family proteins. In RPMI8226 myeloma cells, **imexon** activated caspase-9 and -3 in a time- and concn.-dependent manner. In contrast, cleavage of procaspase-8 was obsd. late and only after exposure to very high concns. of **imexon**. Confocal microscopy confirmed that caspase-3 is also activated after treatment with **imexon**. High **imexon** concns. activated caspase-3 and -9 at 12 h, while caspase-8 activation occurred only at 48 h. **Imexon** cytotoxicity was unchanged in three RPMI8226 cell lines with different levels (low, medium and high) of FAS expression. Similarly, the levels of Bcl-2, Bax and Bcl-x were unchanged in **imexon**-treated cells. However, Bcl-x was translocated to the mitochondria. These data suggest that **imexon**-induced oxidn. activates the intrinsic or mitochondrial pathway of apoptosis, involving cytochrome release and activation of caspase-9 and -3. L L.

CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2003 ACS

2002:845603 CAPLUS

137:337772

Preparation of 2-cyanoaziridine-1-carboxamides by reaction of aziridines with isocyanates followed by treatment with nucleophiles.

Remers, William; Iyengar, Bashyam

The Arizona Board of Regents, USA

U.S., 5 pp.

CODEN: USXXAM

Patent

English

.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6476236	B1	20021105	US 2001-995265	20011126
I US 2001-995265		20011126		

CASREACT 137:337772; MARPAT 137:337772

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EWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
EWS 4 Apr 09 ZDB will be removed from STN
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EWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
EWS 9 Jun 03 New e-mail delivery for search results now available
EWS 10 Jun 10 MEDLINE Reload
EWS 11 Jun 10 PCTFULL has been reloaded
EWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
EWS 13 Jul 22 USAN to be reloaded July 28, 2002;
saved answer sets no longer valid
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EWS 15 Jul 30 NETFIRST to be removed from STN
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EWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
EWS 18 Aug 08 NTIS has been reloaded and enhanced
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now available on STN
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EWS 30 Oct 25 MEDLINE SDI run of October 8, 2002
EWS 31 Nov 18 DKILIT has been renamed APOLLIT
EWS 32 Nov 25 More calculated properties added to REGISTRY
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EWS 34 Dec 04 CSA files on STN
EWS 35 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
EWS 36 Dec 17 TOXCENTER enhanced with additional content
EWS 37 Dec 17 Adis Clinical Trials Insight now available on STN
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EWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003
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EWS 45 Feb 24 PCTGEN now available on STN
EWS 46 Feb 24 TEMA now available on STN
EWS 47 Feb 26 NTIS now allows simultaneous left and right truncation
EWS 48 Feb 26 PCTFULL now contains images
EWS 49 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
WS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002